

Use of the Sentinel Lymph Node to Determine Metastases of Gastrointestinal Malignancies: A Word of Caution

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Identifying the sentinel lymph node has been shown to carry prognostic and therapeutic implications in the surgical treatment of solid tumors. Recently, sentinel lymphadenectomy has been described for gastrointestinal malignancies, but its clinical value remains uncertain. We describe the case of a patient with appendiceal carcinoid who underwent a right hemicolectomy 4 months after appendectomy, out of concern over residual local or regional disease. One sentinel lymph node was identified in the colonic mesentery using the blue dye technique. This sentinel node and 35 others were negative for metastases, but one lymph node not identified through blue dye carried evidence for micrometastatic disease on hematoxylin and eosin (H&E) and immunohistochemical chromogranin stains. The case raises some issues about the value and limitations of sentinel lymph node biopsies in gastrointestinal cancer. Aspects related to technique, learning curve, gastrointestinal lymphatic drainage patterns, the impact of prior operations, and the limited therapeutic implications compared to cutaneous or subcutaneous solid malignancies are discussed. We conclude that at this point in time, the information obtained from biopsies of sentinel lymph nodes during the surgical treatment of gastrointestinal cancer should be utilized with due caution.

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INTRODUCTION

Sentinel lymphatic mapping has received increasing attention in the surgical literature recently. First described by Morton et al. [1] for use in stage I melanoma and later by Giuliano et al. [2] for breast cancer, sentinel lymph node identification using either isosulfan blue dye and/or technetium (⁹⁹Tc) sulfur colloid as imaging agents is emerging as an exciting and important surgical tool for intra-operative assessment of metastatic disease to regional lymph nodes. As with any new modality, a desire to explore its full range of applications exists. Already, sentinel lymphadenectomy for evaluation of metastases has been described in thyroid neoplasms [3], colorectal cancer [4], and others including penile and vulvar malignancies. However, it is important that the initial ex-

citement and enthusiasm for new diagnostic and therapeutic tools be tempered by an appreciation for limitations of the techniques. Although it is too early to identify all of the limitations of sentinel lymphatic mapping, this report serves as a cautionary tale.

CASE REPORT

A 47-year-old woman without prior significant medical problems was found to have urinary stress incontinence, rectal prolapse, and menorrhagia. The patient un-

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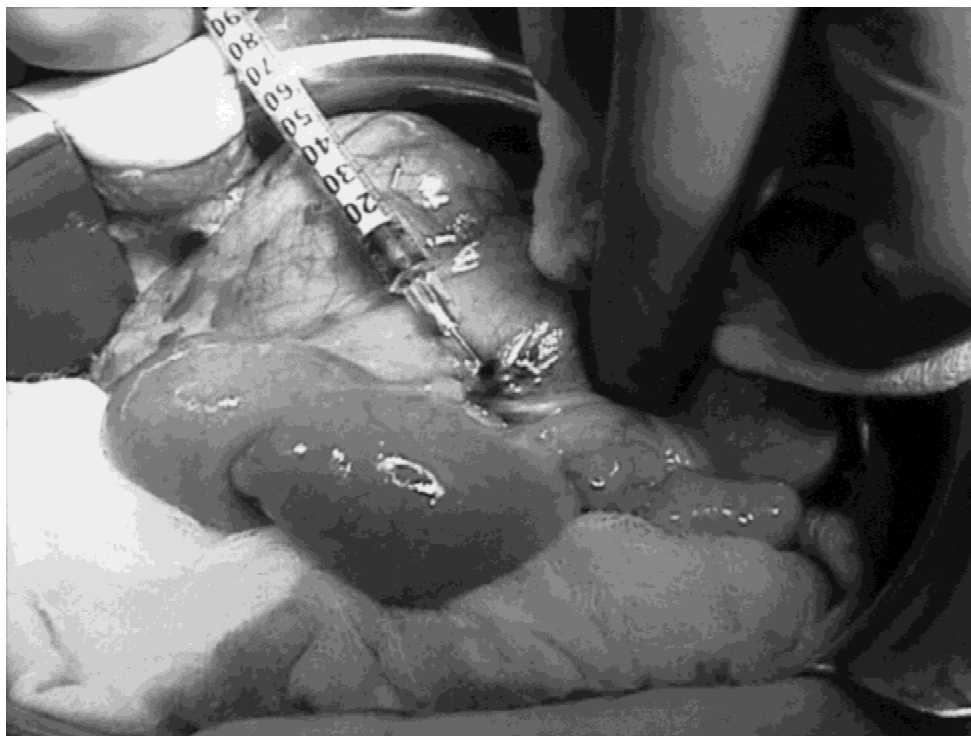


Fig. 1. Isosulfan blue dye injection at the site of the appendiceal stump and mesoappendix.

derwent operative exploration with total abdominal hysterectomy and bilateral salpingo-oophorectomy with a Burch urethral suspension and enterocele as well as posterior vaginal repair. At the time of operation, a mass in the tip of the appendix was noted incidentally, and an appendectomy was performed. Pathologic examination revealed a 1.5-cm poorly differentiated carcinoid in the appendix with extension into the peri-appendiceal adipose tissues with negative surgical margins. The patient presented to our institution for recommendations for further therapy.

At the time of presentation, the patient had an unremarkable physical examination except for a well-healed Pfannenstiel incision from her procedure, with normal laboratory examination. Due to concerns about a possibility of residual regional disease, a right hemicolectomy was performed. Examination of the abdomen revealed no obvious gross disease. After identification of the appendiceal stump, 1 cc of isosulfan blue (Lymphazurin, Hirsch Industries Inc., Richmond, VA) was injected into the subserosa in several regions surrounding the appendiceal stump and at the residual mesoappendix (Fig. 1). One sentinel lymph node was identified in the colonic mesentery (Fig. 2) and was marked with a suture for identification. Subsequently, a right hemicolectomy was performed, including the draining mesenteric lymph nodes in the specimen through high ligation of the ileocolic and right colic arteries. The patient had an uncomplicated postoperative course.

Pathologic examination of the operation specimen revealed no evidence of disease in the right colon or appendiceal stump. Thirty-seven lymph nodes were identified, including the sentinel lymph node. One lymph node had evidence of micrometastatic carcinoid, which was confirmed by immunohistochemical (IHC) identification of chromogranin (Fig. 3). The positive lymph node did not correspond to the sentinel lymph node, which itself revealed no evidence of metastatic disease despite multiple sections examined after hematoxylin and eosin (H&E) and IHC stains.

DISCUSSION

In the 6 years since Morton et al. [1] first published results, according to which identification of the sentinel node as the first lymph node on a direct drainage pathway from a primary cutaneous melanoma accurately reflects the presence or absence of regional metastatic disease in 95% of patients evaluated, there has been an explosion of interest in the application of sentinel lymphadenectomy in a variety of clinical settings. Aside from melanoma, there are data to support the use of this modality in breast [2], thyroid [3], colorectal [4], penile [5], vulvar [6], and oral [7] neoplasms. The main benefit of identifying the sentinel lymph node in gastrointestinal malignancies appears to be the ability to guide histopathologic examinations towards the one structure that carries the greatest likelihood for lymphatic metastasis, therefore facilitating a more precise and possibly more effective staging evalu-

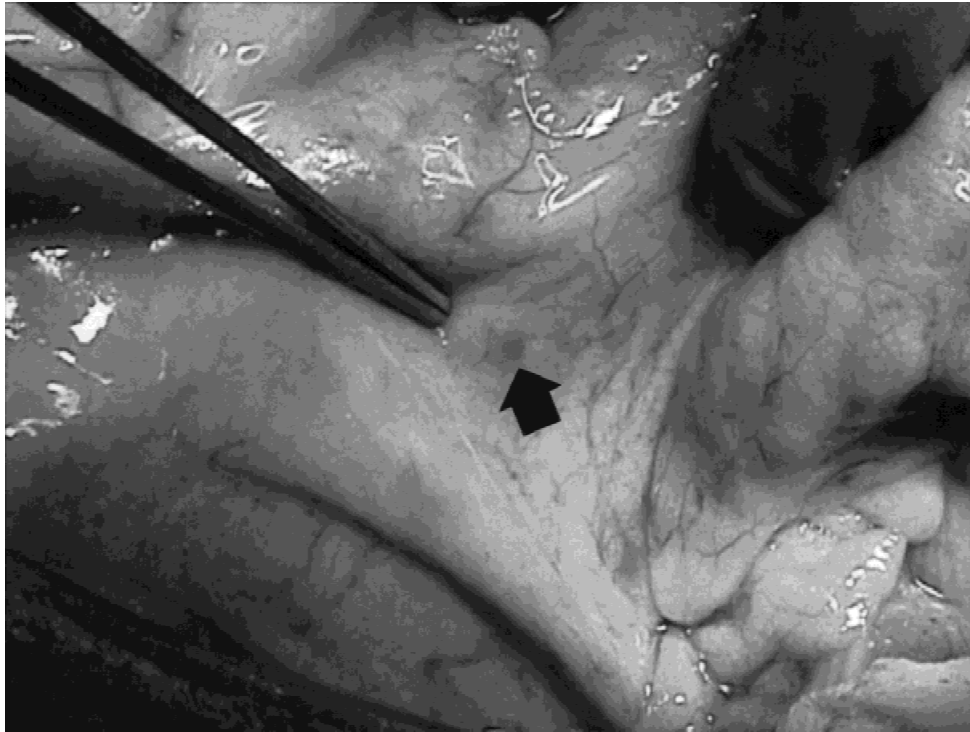


Fig. 2. Sentinel lymph node identified within the mesentery, at tip of forceps (arrow).

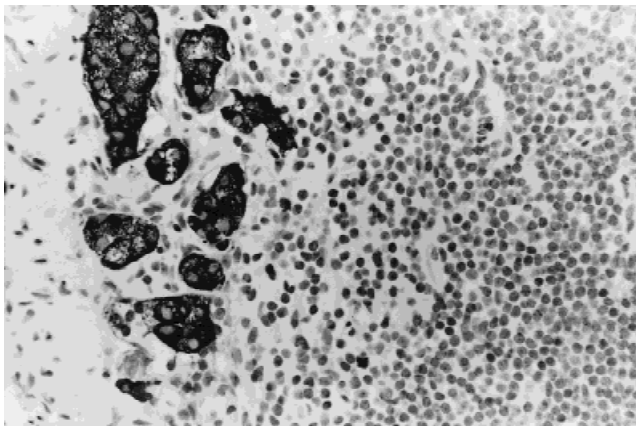


Fig. 3. Immunohistochemical chromogranin stain identifies metastatic carcinoid cells within a mesenteric lymph node. The dark-appearing microscopic clusters of tumor cells are located at the periphery of the lymph node.

ation. Patients “upstaged” in this manner may benefit from additional treatment or a different follow-up regimen. But before one readily embraces this new technique, one must appreciate its limitations, some of which are illustrated in this case report.

One limitation is the often described learning curve associated with this technique. The ability to adequately administer the localizing agent and to identify the sentinel lymph node is likely to be optimized only after performing an as yet undetermined threshold number of cases. As the indications and applications for sentinel

lymphadenectomy expand, the challenge in accurately identifying the sentinel lymph node becomes greater as the surgeon must master an increasing number of technique variations depending on which lymph node basin is being assessed. In this case, it is unclear if the technique of injection, the volume of injected dye, or the anatomic location of injection of the isosulfan blue was appropriate. Was the fact that the sentinel lymph node did not correspond to the histologically positive lymph node due to an error in technique, or was this merely an early point on the learning curve? Only experience obtained through trial-and-error will reveal the answer.

Proper judgment regarding which lymphatic basins are appropriate for application of this technique is vital, as drainage patterns may be unreliable. In this report, the lymph node basin examined is that of the cecum and appendix. If an orderly stepwise progression of the metastatic process can be assumed, lymph node metastases generally spread along the course of the feeding artery of the cancer in the colon. Although branching variations exist, the most constant tributary originating from the superior mesenteric artery is the ileocolic artery [8], which supplies the terminal ileum, cecum, and appendix. In general, lymph node metastases of cecal cancer are preferentially located along the course of the ileocecal artery. It would, therefore, be a relatively safe assumption, that after injection of isosulfan blue around the appendiceal stump, the blue dye should follow a relatively straight and predictable path along this vessel, outlining

a sentinel lymph node. The fact that the sentinel node in our case was indeed not the histologically positive node raises several questions. There is a 1–5% incidence of skip metastases from aberrant lymphatic channels in the large bowel as well as a similar incidence of retrograde metastases to unpredictable sites [8]. Are the drainage basins for gastrointestinal malignancies generally appropriate for evaluation by sentinel lymphadenectomy? Can the technique used for cutaneous lesions, where a reliable segmental-regional lymphatic drainage pattern exists, similarly be applied for use in the gastrointestinal tract? These questions need to be answered for all potentially evaluable sites. In addition, an attempt to identify a sentinel lymph node during a reoperation at any site may turn out to be less accurate, as artifacts in lymphatic drainage patterns may have resulted from the previous operative procedure.

Finally, we must consider what the gain of sentinel lymph node identification in various clinical scenarios is. Will there be less morbidity associated with a less extensive operative procedure prompted by identification of a negative sentinel node? Will we obtain more reliable prognostic information? Would we be willing to postpone a more extensive resection in case of a negative sentinel lymph node at the time of a laparotomy? The answer at this point is likely no, as the morbidity of a more extensive resection certainly appears smaller than that of a second, staged reoperation, a big difference between gastrointestinal and cutaneous or peripheral soft tissue tumors. It seems that in this case of a primary tumor excised under conditions that leave doubts over the proper oncologic extent, this technique, if successful, could have a significant benefit for the patient through better identification of the lymph node at highest risk for

metastatic disease at the time of the appendectomy. Perhaps a formal colon resection could be avoided if a negative sentinel node is reliably identified at the time of operation.

The fact that the sentinel lymph node was not histologically positive and that a lymph node encompassed in the resected colon specimen was positive should be a word of caution. Sentinel lymphadenectomy has to be applied for appropriate indications in the appropriate settings. Further studies will tell us just what these indications and settings are for a more reliable use of this technique in the operative care of gastrointestinal cancer.

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